Genomic Epidemiology of Multidrug Resistant Porcine Commensal *Escherichia coli*

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April 2019

Certificate of Authorship

I, Cameron James Reid, declare that this thesis, submitted in fulfillment of the requirements for the award of Doctor of Philosophy, in the Faculty of Science, School of Life Sciences at the University of Technology Sydney, is wholly my own work unless otherwise reference or acknowledged.

In addition, I certify that all information sources and literature used are indicated in the thesis.

This document has not been submitted for qualifications at any other academic institution.

This research is supported by an Australian Government Research Training Program.

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Date: 8/4/2019

Acknowledgements

Firstly, I would like to thank my supervisors Professor Steven Djordjevic, Dr Piklu Roy Chowdhury and Dr Toni Chapman for their expertise, training, mentorship and support over the course of my candidature. I consider myself privileged to have had your friendship and guidance over the past 4 years. Additional thanks to AusGem, the NSW Department of Primary Industries and the Elizabeth MacArthur Agricultural Institute for providing me with the excellent collection of *E. coli* I was lucky enough to work with.

I would also like to thank all the members of the Djordjevic lab past and present. In particular I would like to thank Ethan Wyrsch and Jess McKinnon for showing me the ropes and training me in the early stages of my Honours and PhD project.

Thank you to Max Cummins, Tiziana Zingali, Priyanka Hastak Shah and Veronica Jarocki. You have been excellent colleagues and friends. You have made the course of my candidature all the more enjoyable and I will always view this time in my life fondly.

Thank you to the academic and technical staff at the i3 Institute, including Director Professor Liz Harry for the supportive and encouraging environment you have created for young scientists. I hope to see the Institute continue to nurture outstanding researchers and make a difference in the world of infectious disease.

I'd like to thank the University of Technology Sydney for supporting me financially with a Doctoral Scholarship as well as the Australian Government Research Training Program.

Finally, and most importantly, I would like to thank my family and friends. My Mum and Dad in particular have been nothing short of amazing in supporting me emotionally and financially throughout this endeavour. I am truly blessed to have such supportive and encouraging parents who have always believed in me. My brother Max has been a rock, a voice of reason and a shoulder to lean on throughout. I love you all.

Statement

This thesis is by compilation. The first two results chapters are published papers listed in the section below. The final chapter is a publication style manuscript that is being prepared for journal submission. Figure and Table numbers have been edited from the original publications to match the chapter numbering of the thesis. Most of the figures are very large and hard to view as they lose resolution due to the margins required within the thesis. Please view the figures as PDFs attached or in the original publications for Chapters 4 and 5.

List of publications

Paper 1; Chapter 4

Porcine commensal *Escherichia coli*: a reservoir for class 1 integrons associated with IS*26.*

Cameron J. Reid[1†], Ethan R. Wyrsch[1†], Piklu Roy Chowdhury[1], Tiziana Zingali[1], Michael Liu[1], Aaron E. Darling[1], Toni A. Chapman[2], and Steven P. Djordjevic[1]

Microb Genom. 2017 Dec; 3(12): e000143.doi:10.1099/mgen.0.000143

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Paper 2; Chapter 5

Australian porcine clonal complex 10 (CC10) *Escherichia coli* belong to multiple sublineages of a highly diverse global CC10 phylogeny.

Cameron J. Reid[1], Matthew Z. DeMaere[1], Steven P. Djordjevic[1]

Microb Genom. 2018 Oct 10. doi: 10.1099/mgen.0.000225

[1]The i3 Institute, University of Technology Sydney, Ultimo, NSW 2007, Australia

Table of Contents

Abbreviations

AMR	Antimicrobial Resistance
ARG	Antimicrobial Resistance Gene
VAG	Virulence-associated gene
MGE	Mobile Genetic Element
IS	Insertion Sequence
DNA	Deoxyribonucleic acid
bp	Base pair
CRL	Complex Resistance Locus
CDS	Calibrated Dichotomous Susceptibility
ESBL	Extended-spectrum beta-lactamase
ESC	Extended-spectrum cephalosporin
AGP	Antimicrobial Growth Promoter
ETEC	Enterotoxigenic *Escherichia coli*
IPEC	Intestinal Pathogenic *Escherichia coli*
APEC	Avian Pathogenic *Escherichia coli*
ExPEC	Extraintestinal Pathogenic *Escherichia coli*
EHEC	Enterohaemolytic *Escherichia coli*
STEC	Shiga-toxigenic *Escherichia coli*
EPEC	Enteropathogenic *Escherichia coli*
aEPEC	Atypical Enteropathogenic *Escherichia coli*
HGT	Horizontal Gene Transfer
MDR	Multiple-Drug (Antibiotic) Resistance
MLST	Multi-locus Sequence Typing
ST	Sequence Type
SNP	Single Nucleotide Polymorphism
WGS	Whole Genome Sequence/Sequencing

Abstract

Swine production is one of the largest agricultural industries in the world. The use of antimicrobials for treatment of disease outbreaks and as growth promoters drives the evolution of antimicrobial resistance in commensal populations of *Escherichia coli* in the pig gut. Therefore, the billions of tonnes of pig faeces generated by production every year are a serious environmental contaminant. Despite the status of *E. coli* as an important commensal and pathogen of both animals and humans, little is known about the genomic characteristics of porcine commensal *E. coli* in Australia. The clonal groups, antimicrobial resistance genes (ARGs), mobile genetic elements (MGEs) and virulence-associated genes (VAGs) they harbour remain poorly characterised.

In order to address this, we characterised 103 multidrug resistant commensal *E. coli* from two Australian farms with a history of antimicrobial use using whole genome sequencing. Phylogroup A and clonal complex 10 strains with global origins and a variety of virulence genotypes associated with extra-intestinal pathogenic *E. coli* (ExPEC) dominated the collection. Multiple class 1 integrons augmented by IS*26,* an important driver of evolution in antimicrobial resistance loci were observed in multiple sequence types. Whilst no resistance to critically important human antimicrobials was observed, this suggests swine production is a reservoir for the evolution of novel drug resistance characteristics that may transfer to human populations and rapidly acquire resistance to critically important antimicrobials.

We also identified an ST131 strain carrying an IncHI2 plasmid with multiple ARGs and a ColV plasmid conferring virulence traits. This strain was highly related to an ST131 strain isolated from a human infection. Remarkably, the human strain carried near identical plasmids. The apparent presence of the IncHI2 plasmid in multiple porcine strains, carriage of metal resistance and identical integrons strongly suggests the human pathogen originated from swine production.

Whilst there is a need to increase the number of porcine commensal *E. coli* whole genome sequences from multiple farms and states in Australia, our findings

support swine production as a reservoir of multiple drug resistance determinants. Furthermore, a proportion of porcine commensal *E. coli* are known or potential human pathogens. Genomic surveillance in swine and other intensively reared food production animals is critical to the ongoing management of the global issue of antimicrobial resistance.